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Clinical letter

Responsive stimulation of motor cortex for medically and surgically refractive epilepsy

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1. Introduction

Epilepsy is a complex disease that evolves throughout patients' lives. For many, seizure management requires escalation from single-drug therapy to multi-drug therapy, adjuvant placement of a vagal nerve stimulation (VNS), and ultimately surgical resection or laser-ablation of the epileptic focus [1]. However, if the seizure focus lies within a region of movement or speech eloquence, lesioning or resection may not be possible without causing neurological deficit. Prior resection may create scarring that prohibits subdural electrode placement. We describe placement of an intracortical responsive neurostimulator (RNS) [2] in motor cortex of a patient whose seizures were refractory to multiple concurrent anti-epileptic drugs, VNS, and prior partial seizure focus resection.

2. Case

A 38-year old right-handed woman presented with a 12-year medically intractable seizure history. Occurring both while awake and during sleep, her seizures were characterized by right-sided hip and knee jerking, intermittently spreading to the right arm and face, with rare generalization to full-body shaking and aphasia (preserving consciousness). Historically, she experienced generalized tonic–clonic seizures as well, but these had been controlled with anti-epileptic drugs (AEDs).

Her seizures were initially managed medically with a combination of AEDs and VNS, which was placed at age 30, but removed 6 years later for lack of benefit. At age 36, she averaged 8 seizures daily, and subdural electrocorticography (ECoG) electrodes were placed for seizure focus localization (Fig. 1 panels A and C). Seizure onset localized to interhemispheric left Rolandic cortex, overlapping with leg motor architecture (identified by electrocortical stimulation; ECS). She underwent conservative resection, resulting in transient right lower-extremity paresis (distal > proximal). Pathology showed "small foci of giant neurons", but did not show overt evidence of cortical dysplasia. Her proximal strength and ambulatory function slowly improved, although without dorsiflexion at the ankle or great toe. Her seizures ceased (Engel-class 1) for ~2.5 years following resection.

At age 38, her seizures returned with the same semiology, with jerking of the right leg, lasting 15–25 s (electrographically) in length, quickly increasing in frequency to ~5 daily. Inpatient continuous EEG did not reveal an expanded ictal onset zone, but it was felt that the focus was within sensorimotor cortex surrounding the previous resection. It was felt that the risk for operative morbidity with a craniotomy for repeat placement of subdural grids and strips in the area of prior surgery was too great, due to extensive adhesions and scarring of the pia with the dura and vasculature. Given her weakness following resection, additional resective surgery was not entertained due to expected functional deficit, and RNS was considered instead. Frameless, stereotactically guided, RNS depth electrode trajectories were planned based upon careful review of prior functional-ECS, epileptiform ECoG findings, anatomy of the prior resection, and diffusion tractography (Fig. 1 panel E). Two 4-electrode RNS leads were placed anterioventrally and posteroventrally at the boundaries of the prior resection cavity, with 4/8 contacts likely within primary motor cortex (Neuropace, Mountain View, CA). The responsive neurostimulator was activated on post-operative day 2, and, within a month, her seizure frequency decreased from her pre-operative baseline of ~5/day to ~2–3/week. These residual seizures are characterized by milder sensorimotor semiology, lasting 5–7 s electrographically. This reduction has remained stable for >9 months post-operatively to date with no evidence of paresthesias nor other untoward side effects (Engel class 3). Telemetric physiology demonstrates that seizures are being successfully identified and aborted with stimulation (Fig. 1 panel F).

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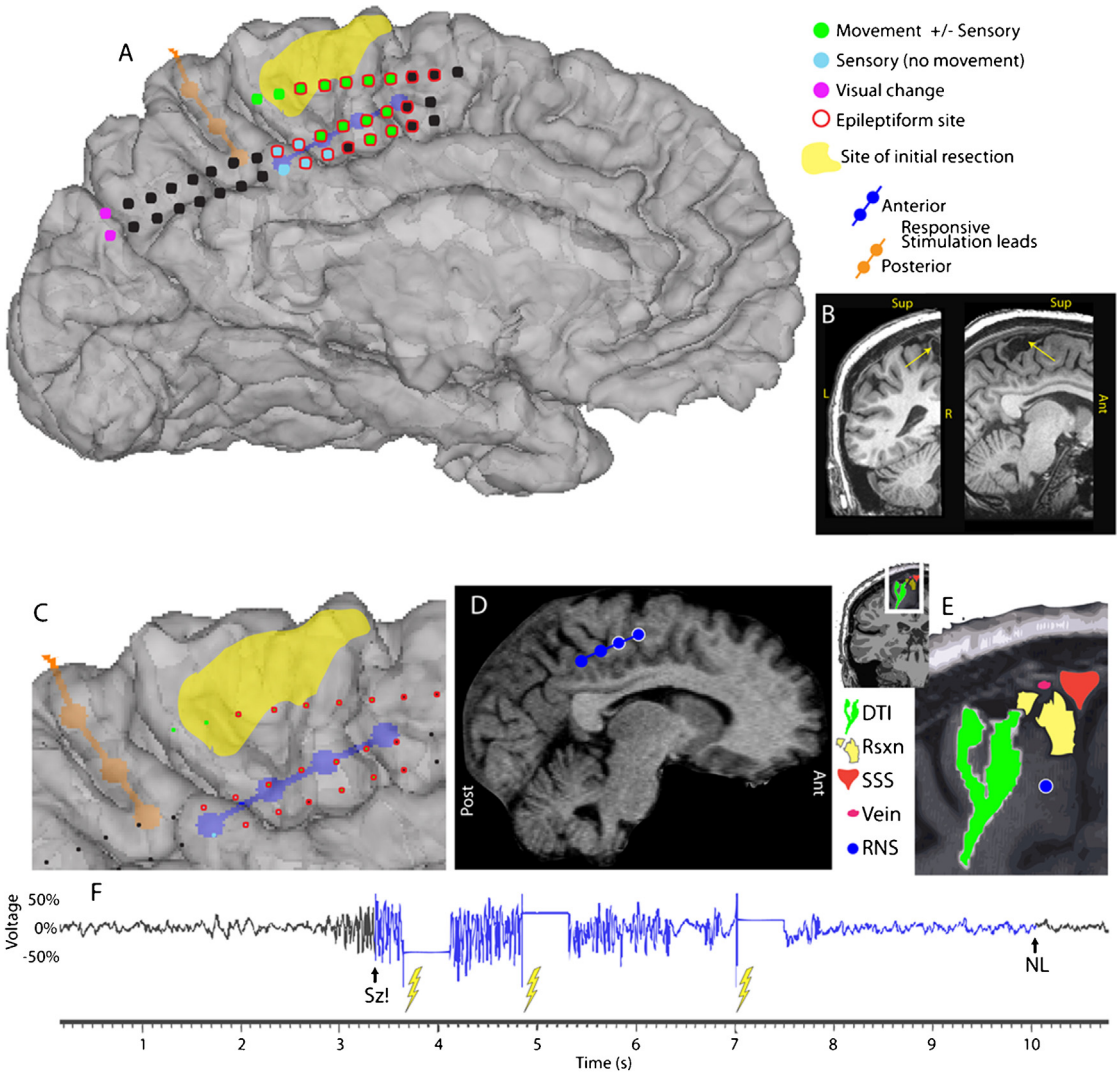

Fig. 1. (A) The patient's left hemisphere is viewed from a medial perspective. Lateral surface ECoG electrodes (from 3 years prior to RNS placement [2]) demonstrate regions of ECS-induced movement and sensation of the right lower extremity, or visual change. Epileptiform electrodes are red-circled. The yellow shading indicates resection bed (from 3 years prior). Within the semi-transparent cortical rendering, the anterior (blue) and posterior (orange) RNS leads can be seen within the brain. (B) Resection bed (yellow arrows). (C) Expanded view of (A), illustrating RNS lead location (ECoG size reduced). (D) Sliced cortical section through anterior RNS lead, after rotating about axial plane. (E) Given prior resection bed and adjacent structures, stereotactic depth placement optimized safety and localization to focus. (DTI: tractographic localization of corticospinal tract; Rsxn: resection; SSS: superior sagittal sinus; Vein: large cortical vein). (F) Voltage tracing of differential-pair (white circled cites in D) during detected seizure interval (blue tracing – seizure start marked with "Sz!", return to normal at "NL"). Flashes indicate 3 stimulations through this electrode pair.

3. Discussion

Medically refractory seizures originating from motor cortex present a particularly difficult clinical challenge. Even with the best pre-operative and intraoperative mapping, surgical resection or stereotactic laser ablation represent a forced compromise between extent of treatment and risk of functional deficit [3]. As with our patient, limited resections that attempt to preserve function can result in functional morbidity with continued seizures. Therefore, stimulation of the motor cortex to arrest seizure initiation and propagation represents an attractive alternative.

Continuous paddle-style surface stimulation of motor cortex seizure foci has been reported in several patients, with reduction in seizure frequency [4]. While these cases suggest promise, RNS has the added benefit of minimizing stimulation-related side effects, and conserving power [2,4]. In this case, surface electrodes were contraindicated because of scarring and surface irregularity from the previous resection, adjacent vasculature, and the transient paresis following initial resection. Continuous stimulation [4], which may have different efficacy, has not yet been approved for use in the United States. In our patient, RNS using intracortical depth electrodes has proven its ability to identify and abort primary-motor cortical seizures, markedly reducing reported seizure frequency without sensorimotor side-effect. Use of depth electrodes allowed safe avoidance of prior resection site and vulnerable anatomic structures. We propose that RNS be considered as a possible therapy in cases of medically refractory epilepsy with a seizure focus within eloquent cortex.

Conflicts of interest

None.

Disclosures

All authors declare no disclosure relevant to the manuscript.

Author contributions

KJM, GAG and CHH prepared the study concept and design. All authors contributed in drafting/revising the manuscript.

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